

SUB
BY
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COO-4.
U.S. Application No.: 09/876,830

unsubstituted aryl and heteroaryl, (unsubstituted aryl)-(C₁-C₄)alkyl, and (unsubstituted aryl)oxy-(C₁-C₄)alkyl.

REMARKS

Claims 1-25 were pending in subject application. Claims 1-25 have been cancelled in favor of new claims 26-41 which are being added by the present amendment. As discussed below, no new matter has been added by way of this amendment.

Election/Restrictions

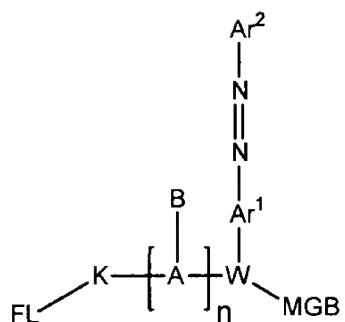
The Examiner has taken the position that the application is claiming two distinct inventions, namely:

Group I: Claims 1-20, drawn to oligonucleotide probe; and

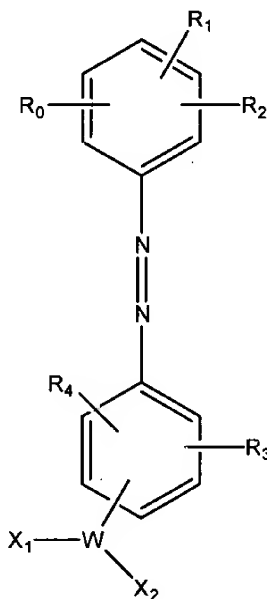
Group II: Claims 21-25, drawn to method of hybridizing.

The Examiner has required election between these two groups of claims, and furthermore requests that a specific structural representation (e.g., selection of specific A, Ar¹, Ar², etc. groups as recited in the claims) as well as a chemical name be provided to expedite prosecution.

In reply, Applicants elect to prosecute the subject matter of Group I, namely, the subject matter of claims 1-20 amended as set forth in claims 26-41, as explained below. Claims 1-10 are directed to oligonucleotide probes as described by the following chemical formula

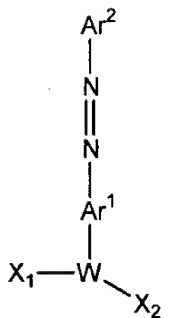


Claims 11-16 are directed to a preferred embodiment of reagents that may be used in preparing the probes of claims 1-10, namely reagents described by the following chemical formula



In response to the restriction requirement, Applicants are electing to prosecute claims directed to reagents useful in the preparation of the probes of claims 1-10. However, rather than prosecute claims to a preferred group of these reagents as set forth in claim independent claim 11, Applicants submit for examination claim 26 and claims dependent thereon, which are directed to reagents commensurate in scope with the probes of claim 1. Support for the subject matter of claim 26 and claims dependent thereon is found throughout the application.

More specifically, claim 26 is directed to the quencher reagents which have the formula



In claim 26:

X_1 is defined as set forth at page 20, lines 15-18 as a group selected from H, $(\text{C}_1\text{-C}_{12})$ alkyl, aryl, heteroaryl, and protected or unprotected functional group;

X_2 is defined as set forth at page 20, lines 18-19 as any phosphorus coupling moiety used in oligonucleotide synthesis, and is also defined at page 25, lines 6-12 within the scope of the $-\text{R}_6\text{-C=O-X}_3$ as groups that are reactive towards nucleophiles (where phosphorus coupling moieties are exemplary), so that X_2 in the above structure is defined within the claim as a moiety reactive towards nucleophiles;

W is defined as set forth at page 20, lines 14-15 as a linking group having from 3 to 100 backbone atoms selected from C, N, O, S, Si and P, said linking group being cyclic, acyclic, aromatic or a combination thereof; and

Ar^1 and Ar^2 are each defined as set forth at page 6, line 1 as being a substituted or unsubstituted aryl group, where these terms are defined at, e.g., page 16, line 25 to page 17, line 23.

Claim 27 is directed to reagents according to claim 26 wherein X_1 is selected from the group consisting of OH, O-dimethoxytrityl, O-methoxytrityl, O-trityl or an oxygen atom having an acid labile blocking group, as disclosed in claim 13. Claim 28 is directed to reagents of claim 26 wherein X_2 is selected from the group consisting of a phosphorous coupling moiety, a pentafluorophenoxy moiety and a succinimidyl

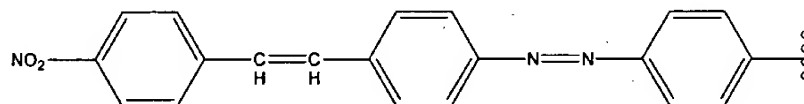
moiety, as disclosed at page 25, lines 9-12. Claim 29 is directed to reagents of claim 26 wherein X_2 is a phosphoramidite, e.g., a group of the formula $-O-P(N(iPr)_2)(OCH_2CH_2CN)$, as disclosed at page 9, line 18. Claim 30 is directed to a compound of claim 26 wherein $-W(X_1)(X_2)$ is $-N(CH_2CH_2Ra)(CH_2CH_2Rb)$ and Ra and Rb independently represent a functional group or a protected functional group for attaching the quencher to a linking group or conjugate, as disclosed at page 27, lines 6-10 and in the specific compounds drawn in Table 1 that bridges pages 27 and 28. Claim 31 is directed to compounds of claim 26 wherein $-W(X_1)(X_2)$ is $-N(CH_2CH_2OH)_2$, as disclosed by many of the compounds in Table 1 (pages 27 and 28) and as disclosed at page 30, lines 3-6.

Claim 32 is directed to reagents of claim 26 wherein one of Ar^1 and Ar^2 is directly or indirectly substituted with a substituted aryl group (Ar^3), where Ar^3 extends the resonance ability of the $Ar^1-N=N-Ar^2$ aromatic system and thereby increases the wavelength absorbance maximum of the compound, as disclosed at page 17, lines 20-23. The term " Ar^3 " has been added for convenience to give a specific name to the "another substituted aryl group" that functions to "extend the resonance ability of the aromatic ring system" as referred to in the cited excerpt of the application. Claims 33-36 are directed to the various options encompassed within the scope of this definition, namely, where Ar^1 is directly substituted with Ar^3 (claim 33), Ar^1 is indirectly substituted with Ar^3 (claim 34), and Ar^2 is directly substituted with Ar^3 (claim 35), and Ar^2 is indirectly substituted with Ar^3 (claim 36).

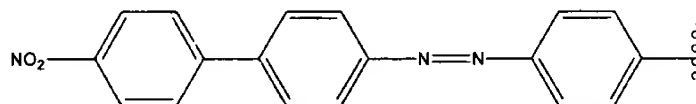
Groups useful to achieve indirect substitution of an Ar^3 group are claimed in claims 37 and 38. Claim 37 is directed to reagents wherein Ar^1 or Ar^2 is indirectly substituted with Ar^3 through a group selected from $-(C\equiv C)_n-$ and $-(CR'=CR')_n-$ where n is 0 to 5 (as disclosed at page 17, lines 22-23) and R' is independently selected from hydrogen, (C_1-C_8) alkyl and heteroalkyl, unsubstituted aryl and heteroaryl, (unsubstituted aryl)- (C_1-C_4) alkyl, and (unsubstituted aryl)oxy- (C_1-C_4) alkyl (as disclosed at page 17, lines 6-8). Claim 38 is directed to reagents wherein Ar^1 or Ar^2 is indirectly substituted with Ar^3 through a double bond selected from carbon-carbon and nitrogen-nitrogen

double bonds, as disclosed at page 17, lines 22-23 and the first entry in Table 2 at page 28 (illustrating aryl-aryl group connections by both carbon-carbon and nitrogen-nitrogen double bonds).

Claim 39 is directed to a specific quencher structure, as exemplified at page 28, Table 2, first entry, having the structure:

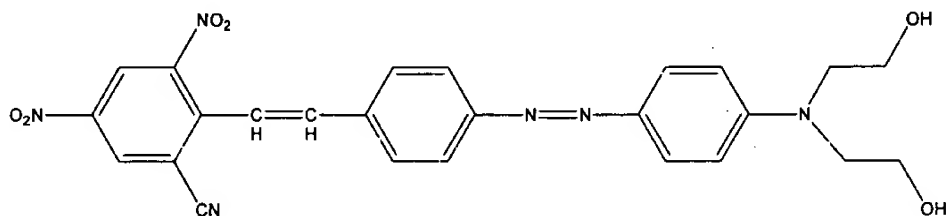


Claim 40 is directed to a specific quencher structure, as exemplified at page 29, Table 2, first entry, having the structure:

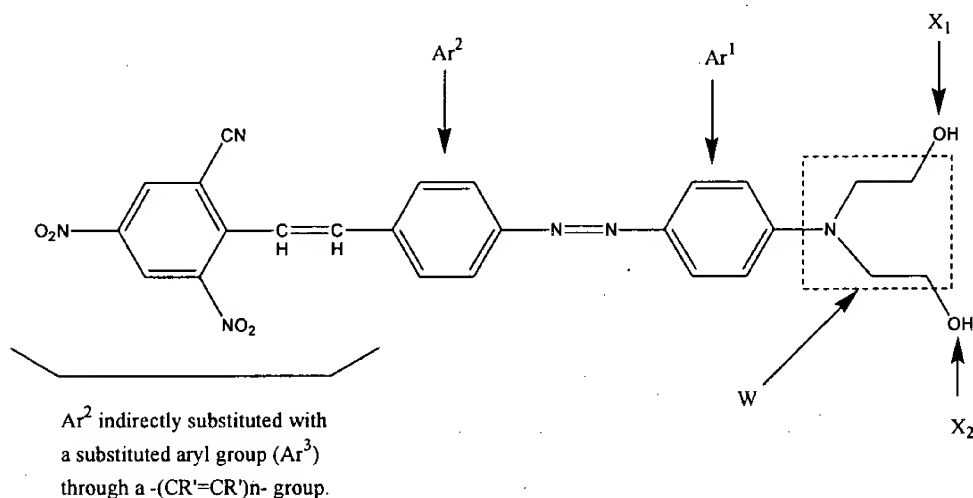


Claim 41 is directed to further defining the "substituted aryl groups" present in the reagent compounds of claim 26, where the definition finds support at, for example, page 17, lines 1-8.

The Examiner has requested that a specific compound be elected in order to expedite prosecution. To this end, Applicants elect the compound as set forth in Table 2, first line, on page 28 of the application, *i.e.*, a compound having the quencher moiety of claim 29 and the linking moiety of claim 31, *i.e.*,



In the terms of claim 26, and as shown on the following page, in this structure Ar^1 is a phenyl group that is unsubstituted except for X_1-W-X_2 and $-N=N-Ar^2$; Ar^2 is a phenyl group that is indirectly substituted with a substituted aryl group (Ar^3 according to the language of claim 29), where Ar^3 is substituted with nitro and cyano, and $CH=CH$ provides the indirect substitution between Ar^2 and Ar^3 , and X_1-W-X_2 is $-N(CH_2CH_2OH)_2$ (i.e., X_1 and X_2 are each OH, and W is $-N(CH_2CH_2-)_2$).



At the moment, Applicants are unable to provide the name of this compound as requested by the Examiner. However, Applicants will quickly try to obtain the name and advise the Examiner accordingly.

The Commissioner is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned **"Version With Markings to Show Changes Made."**

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Entry of the Amendment, and an early examination of the application and pending claims are earnestly solicited. Should any issue require attention prior to examination, the Examiner is requested to contact the undersigned at (206) 622-4900 to resolve the matter.

Respectfully submitted,
Seed Intellectual Property Law Group PLLC



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Registration No. 32,783

DWP:scc

Enclosures:

Postcard
Check for \$200
Petition for Extension of Time
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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claims 1-25 have been canceled.

New Claims 26-41 have been added.